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ARTIGO DE REVISÃO/REVIEW ARTICLE

Um perfil clínico da pneumonia estafilocócica em toxicómanos

A Clinical Profile of Staphylococal Pneumonia on drug addicts

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RESUMO

Objectivo: rever o perfil clínico dos doentes com Pneumonia por *Staphylococcus aureus* no Serviço de Pneumologia do Centro Hospitalar Conde S. Januário.

Desenho: análise retrospectiva.

Métodos: foram revistos os processos clínicos e radiológicos bem como os resultados bacteriológicos e a resposta à terapêutica de todos os doentes internados, num Serviço de Pneumologia, com o diagnóstico de pneumonia por estafilococos, durante o período compreendido entre 1991 e 1994.

ABSTRACT

Objective : To review the clinical profile of patients with Pneumonia due to *Staphylococcus aureus* at the Pneumology Service of Centro Hospitalar Conde S. Januário.

Design: A retrospective analysis.

Methods: The case notes, the chest radiographs, the microbiology results and the response to therapy of patients with staphylococcus pneumonia, admitted at the hospital for a period 1991-1994, were reviewed.

Results: A total of 10 males patients, with mean age 27,9 year (range 16 to 34 years) were notified as

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Resultados: um total de 10 doentes, todos do sexo masculino, com uma média de idades de 27,9 anos (16-34), com o diagnóstico de pneumonia estafilocócica foram analisados. Todos eles (100%) eram toxicomanos por via parentérica. Tosse, dispneia, febre, astenia e anorexia foram as manifestações clínicas predominantes. Infiltrados bilaterais multiplos e pneumatocelos, na radiografia de tórax, ocorreram em todos os doentes. Três doentes tiveram como complicação endocardite, três com pneumotórax, dois com derrame pleural, dois com insuficiência renal aguda e um com insuficiência hepática. O Staphylococcus aureus foi isolado em hemoculturas de todos (10/10) os doentes e em expectoração de apenas dois (2/4). Todas as estirpes eram sensíveis aos derivados semi-sintéticos da penicilina. Todos os doentes registaram desaparecimento da sintomatologia e melhoria radiológica após antibioterapia.

Conclusões: os toxicómanos que utilizem a via parentérica constituem um grupo de risco para bacteriémia estafilocócica, infecção da valvula tricuspida e pneumonia bilateral.

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Palavras- chave: *Staphylococcus aureus*; Toxicómano, Pneumonia; Endocardite; Penicilina semi-sintética

having staphylococcus pneumonia between 1991 and 1994. All of them (100%) were intravenous drug addicts. Cough, dyspnea, fever, fatigue and anorexia were the predominant clinical manifestations. Multiple bilateral infiltrates and pneumatoceles on the chest radiograph occurred on all of the patients. 3 patients were complicated with endocarditis, 3 with pneumothorax, 2 with pleural effusion, 2 with acute renal failure and one with liver failure. The *staphylococcus aureus* was isolated from the blood culture in all patients (10/10) and 2 (2/4) from the sputum cultures. All strains were semisyntetic penicillins sensible. All the patients had complete resolution of the symptoms and improvement in the chest radiograph findings after antibiotic therapy.

***Conclusions:* Drug addicts who use parenteral routes are especially prone to Staphylococcal bacteremia, tricuspid valve infection, and bilateral pneumonia.**

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Key-words: *Staphylococcus aureus*; Drug addicts; pneumonia; endocardites; Semisyntetic penicillin

INTRODUCTION

Community acquired pneumonia is a serious illness, associated with significant morbidity and mortality (1) and have a significant impact on the health care system. Staphylococcal pneumonia is fairly uncommon but very serious (2) and associated with a high mortality (30-40%) even with appropriate therapy (3,4,5). Therefore, the preantibotic era's mortality rates of more than 90% decrease dramatically (6).

The *Staphylococcus aureus* is the second most common infectious agent of pneumonia in the ICU (7). This organism produces a large array of enzymes and toxins that contribute to the remarkable pathogenicity (8) that result in severe damage to lung tissue. *Staphylococcus aureus* infects the lungs by the aerogenous or hematogenous route. The aerogenous route is the classic one and is similar to the way in which most other types of pneumonia. There is an increased incidence *of Staphylococcus aureus* pneumonia in patients who suffered a recent bout of influenza (7), and in older patients (than 50years) with one or more underlying diseases.

However, hematogeneous pulmonary infection is not uncommon and is often severe especially in hospitalized patients (6).

The skin is the major site of entry of hematogeneous spread *of Staphylococcus aureus* to the lungs through bacteremia, which ensues as a result of one of a variety of disease processes. It was reported to occur in association with skin and soft tissue infection(9), burns (10), pyomyositis, infected intravenous catheter, valves prostheses, dialysis shunts, and in drug addicts who use parenteral routes (9,11,12,13). These are

especially prone to staphylococcal bacteremia, renal, splenic or bone abscesses, endocardites, and pneumonia (14,15).

Perhaps relevant is the observation that drug addicts have higher staphylococcal carrier rates for nose and skin than does the population at large.

Often, the diagnosis is clear: shaking chills, remittent (or intermittent) fever in a patient with a skin wound or evident source of staphylococci followed by symptoms referable to the respiratory tract and pulmonary infiltrates. Cough, purulent sputum, and chest pain are common. Hemoptysis may occur, "dirty salmon pink" sputum is not typical for this disease. The classical radiographic findings are that of bilateral bronchopneumonia and necrosis, leading to early excavation and the formation of thin-walled lung abscesses. The complications of intrathoracic infection are exceedingly diverse because of the widespread foci: focal pneumatocele formation and subpleural emphysema are sometimes stinking; bronchopleural fistula with pyopneumothorax, pleural effusion and empyema are common. Endocardites with tricuspid valve evolvement without a history of prior heart disease is a well-recognized complication of staphylococcal hematogeneous infection of drug addicts (14). In this patients a history of prior heart disease is usually absent and the incidence of tricuspid valve involvement, otherwise very low, approximates 50% (16).

Multiple blood cultures drawn before the initiation of therapy are extremely important in patients with suspected staphylococcal bacteremia.

Between 1991-1994 we review the patients that was admitted in the ward of Pneumology Department, with the diagnosis of Staphylococcal Pneumonia.

MATERIAL AND METHODS

All registered admissions in the Pneumology Service of Centro Hospitalar de Conde S. Januário, since January 1991 to December 1994, were retrospectively reviewed in detail with the clinical charts. Patients with staphylococcal pneumonia were identified. Data were collected on age, sex, interval (days) between the onset of symptoms and the admission in the hospital, smoking and alcoholics habits (daily alcohol ingestion > 80g), intravenous drug addiction, underlying diseases, laboratory findings, radiologic features, complications, microbiologic specimens and therapeutic outcome.

RESULTS

Patient population

From 1 January 1991 to 31 December 1994 a total of 1747 patients were admitted in the Pneumology Service of Centro Hospitalar de Conde S. Januário. Of the 48 (2,7%) patients with hospital discharge diagnosis of community-acquired pneumonia,10 patients suffered of Staphylococcal pneumonia. The 10 patients, that consisted the study population, were men, with a mean age of 27.9 years (range 16 to 34 years). The racial distribution included one Caucasian and 9 Chinese patients.

All of patients were intravenous drug addicts with an average duration of drug abusing of 9 years (range 8 months to 14 years). Four referred smoking habits and all ten patients had no underlying diseases or alcohol abuse.

Duration of hospital stays range from 19 to 39 days with a mean stay of 29.5 days.

Clinical presentation

The median duration of respiratory and constitutional symptoms before the admission was 8.3 days (range 5 to 20 days). The onset of illness was typically acute with defining initial event. The most common initial respiratory symptom was cough, which was present in all patients; cough was productive in 9 of patients and bloody sputum appeared in 4 patients. The second most common respiratory symptom was dyspneia that occurred in 8 patients. Chest pain was

present in only one patient. High-grade fever, anorexia and generalized weakness were the prevalent constitutional symptoms that were reported in all ten patients. Weight loss occurred in two patients (Table 1).

TABLE I

Symptoms of presentation in 10 drug addicts patients with *Staphylococcus aureus* pneumonia

Symptoms	N° of Pts
Respiratory	
cough	10
productive	9
dispnea	8
hemoptysis	5
chest pain	1
Constitutional	
fever	10
anorexia	10
fatigue	10
weigth loss	2

Laboratory findings

Nine patients were anemic (Hct < 40 percent) and the majority was classified normochromic and normicitic. The ESR ranged from 62 to 115 mm/h. Thrombocytopenia (<100.000/mm^3) was observed in three patients. Ten patients had leucocytosis with a mean of 15.860 /mm^3 of peripheral white blood cell count. Creatinine concentration was increased (> 125µmol) in two patients and hyponatremia was referenced in seven (70%) patients.

Hyperbilirubinemia and hypoalbuminemia (<30g/L) was encountered respectively in five (50%) and six (60%) patients. None of the ten patients was infected with HIV.

Five patients revealed hipoxaemia that range from 59 to 73 mmHg and four of these with hypocapnea ($PaCO_2$<32mmHg).

The appearance on the chest radiographic was similar for the 10 patients. Diffuse patchy areas of infiltrates and multiple bilateral areas of cavitation (pneumatoceles) were seen on admission. Three (3/10) patients had associated pneumothorax and two (2I10) pleural effusions, that no turn out to be empyema.

In five patients with murmur examined by echocardiography three had demonstrable vegetation on the tricuspid valve.

All of the ten (100%) patients had positive blood cultures for *Staphylococcus aureus*. The sputum culture was positive in three patients and one of them yield more than one pathogen; in one patient the *Staphylococcus aureus* growth on the urine culture. All the Staphylococcus aureus isolates were penicillin resistant.

Treatment

All patients received empiric initial antibiotic therapy, tacked into account the clinical and epidemiological history, and the chest radiograph findings with previous collect of samples for blood, sputum and urine culture.

One the initial, five patients received a penicillinase-resistant penicillin, three patients was treated with vancomycine, one with a third-generation cephalosporin and another with erytromicine. Combination therapy was used in six patients: in 5 patients added with an aminoglycoside and one with a third-generation cephalosporine.

Changing of antibiotic therapy occurred in 3 patients: one patient that had made erythromycin during two days changed to a penicilinase-resistant penicillin after staphylococcus aureus was recovered from blood culture; one patient that had received a third-generation cephalosporin and another treated with a penicilinase-resistant penicillin were changed to vancomycine because revealed allergic to penicillins derivate. The three patients that had vegetations on the tricuspid valve detected by echocardiography was treated with a penicilinase-resistant penicillin or vancomycine associated with aminiglycoside.

The length of treatment was between 3 and 6 weeks.

In all patients the medical treatment was successful with a complete clinical resolution and improvement of the chest radiographs findings.

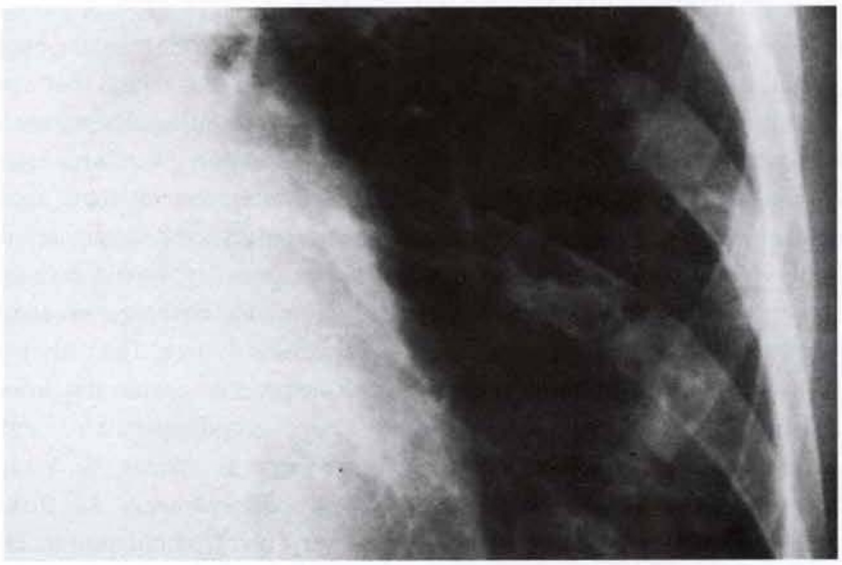

Fig. 1 – Chest radiograph from 22 year-old man drug addict with staphylococcal pneumonia (pneumatoceles)

DISCUSSION

The epidemiology of staphylococcal pneumonia was first scrutinized during the preantibiotic era by Chikering and Park in 1919 (17). They reported 155 patients who developed *Staphylococcus aureus* pneumonia after an influenza outbreak. During 1950, authors focused on differences between adult and pediatric patients with staphylococcal pneumonia (18). *Staphylococcus* was responsible for 15% of primary pneumonia, which was a notable increase from prior reports (19). Recent adult community-acquired cases have followed influenza in 52% of cases (20). A substantial percentage of these patients were tobacco and alcohol users, and half preexisting chronic diseases.

Recent articles support the distinction between aerogenous and hematogenous staphylococcal pneumonia (9,21). In less developed areas of the world, the hematogeneous variety continues to be seen in the setting of skin and soft tissues infections (22). In the United States, the source of bacteremia is more typically from tricuspid valve endocardites related to intravenous drug abuse, intravascular catheters, or hemodialysis (9).

Data collected from our retrospective study of 48 patients admitted to the Pneumology Service of CHCSJ for community-acquired pneumonia, between 1991 and 1994, ten (20.8%) fulfilled the criteria for staphylococcal pneumonia. All of 10 patients were young men and intravenous drug addicts.

Intravenous drug abusers are an important risk group for acquiring HIV. None of our patients was infected with HIV or had underlying disease.

The illness, before diagnosis, had a mean duration of 8.3 days that was similar than the review of Chambers et al (23).

When first seen our ten patients, the criteria of sepsis and bacteremia (24) were fulfilled respectively by seven (70%) and three (30%) patients.

Bilateral septic pulmonary embolus was observed in all 10 (100%) patients, suggested by the chest radiograph findings that showed multiple and bilateral infiltrates and cavitation (pneumatoceles).

Staphylococcal endocardites is a condition affecting intravenous drug abusers at increasing rates (15). *Staphylococcus aureus* may attack normal or damaged native valves, or prosthetic valves, and has predilection for the tricuspid valve in drug addicts (25). Julander

et al (26) consider that the triad drug addiction-staphylococcal septicemiapulmonary embolism is pathognomonic for tricuspid valve endocardites. Consequently, patients fulfilling these criteria should be treated as suffering from endocardites, although no significant murmur can be heard or the echocardiography had no consistent with tricuspid valve endocarditis.

In our study, five patients with staphylococcal pneumonia and murmur examined by echocardiograph, only three had vegetation on the normal native tricuspid valve. *Staphylococcus aureus* bacteremia may be a cause or a result of pneumonia (9,27) and the blood culture in the appropriate clinical setting provide the cause of pneumonia (7). All of the ten (100%) patients we studied had positive blood culture for *Staphylococcus aureus.*

Treatment of staphylococcal infection requires selection of optimal therapy based on susceptibility testing, antimicrobial pharmacokinetics, and consideration of therapeutic index of the selected antimicrobial drugs (7). The semisynthetic penicillins are the most active agents against strains of penicillinase producting that compose more than 90% of strains of staphylococcus aureus isolated. The majority of community-acquired staphylococci are penicillin resistant (3). Therefore, initial therapy is semisynthetic penicillin.

All of isolates of staphylococcus aureus in our study were penicillin-resistant, but β- lactam-sensitive.

Agents in this class that considered first line antistaphylococcal agents include methicilin, oxacillin and flucloxacillin given intravenously in large doses. Other β-lactamase-resistant agents, including the cephalosporins and β-lactamase inhibitors can be used in the treatment of *Staphylococcus aureus* pneumonias, if broader coverage of aerobic and anaerobic organisms is desired. The activity of third-generation cephalosporin is considerably lower than that of either first or second-generation cephalosporin against *Staphylococcus aureus* (7). With β-lactam-resistant *Staphylococcus aureus* the treatment of choice is vancomycine. Combination therapy is usual, like in our study, but has not been shown affect morbidity or mortality (25) . With mono or combination antimicrobial therapy, our ten patients achieved clinical and microbiologic cure, without severe complications.

We can offer the following conclusions:1) *Staphylococcus aureus is* uncommon but very serious infection; 2) the skin is the major site of entry of hematogenous spread of staphylococcus to the lungs; 3) drug addicts who use parenteral routes are prone to staphylococcal bacteremia/sepsis, endocardites and pneumonia; 4) the medical treatment with antistaphylococcal agents had proved to be effective to treat staphylococcal pneumonia in drug addicts complicates with endocardites.

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